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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/719,311 | 11/20/2003 | John A..Chiorini | 14014.0252U3 | 3284 |

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| EXAMINER |
|---|
| KAUSHAL, SUMESH |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 03/22/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/719,311 | CHIORINI ET AL. | |
| | Examiner | Art Unit | |
| | Sumesh Kaushal Ph.D. | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's response filed on 12/20/06 and 09/26/06 has been acknowledged.

*Claims 1-42 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

### *Claim Rejections - 35 USC § 112*

Claims 1-42 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 06/28/06.

The scope of invention as claimed encompasses a recombinant genetic material (vector system for producing virus particles) encoding AAV4 capsid protein. The scope of invention as claimed further encompasses variant of AAV4 Rep proteins (SEQ ID NO(s): 2, 8, 9, 10 and 11) and AAV4 Capsid proteins (SEQ ID NO(s): 4, 16 and 18) which are only 95-98% identical to the disclosed representative ptoeirns. Besides the nucleotide sequence of SEQ ID NO:1 which encodes AAV4 genome, AAV4 Rep proteins (SEQ ID NO(s): 2, 8, 9, 10 and 11) and AAV4 Capsid proteins (SEQ ID NO(s): 4, 16 and 18) the specification as failed fails to disclose any variants of AAV4 Rep and capsid proteins. In addition besides the nucleotide sequence of SEQ ID NO:1 which encodes the AAV4 genome, the speciation as field fails to disclose any other vector for

producing infectious virus particles having characteristic of AAV4 that contains any and all characteristic of AAV4.

**Response to Arguments (Written description)**

The applicant argues that the instant disclosure was sufficient to enable one of skill in the art to prepare a vector system having the desired tissue tropism of AAV4. the applicant argues that it is explicitly taught in the specification (pg. 42, line 17) that it is the differences in capsid proteins that are relevant to the differences in hemagglutination and tissue tropism between AAV4 and other adeno-associated viruses (AAVs). The applicant argues that based on applicants publications regarding the distinctions between AAV4 and AAV2, it is generally accepted by those skilled in the art that the capsid proteins of AAV vectors are the elements that would convey these characteristics. The applicant argues that in view of state of the post filing art one ordinary skill in the art would recognize that the AAV4 capsid proteins are what contribute to the unique properties of AAV4. Regarding the sequence variation the applicant further argues that invention as claimed (i.e. 95-98% sequence variation) are according to the USPTO written description guidelines. The applicant further argues that in the case of AAV4 Rep and capsid variants, it is routine experimentation for one skilled in the art to test such variants to determine if they fit into the claimed homology and function by assaying the ability of a vector system to replicate and produce encapsidated particles.

However this is found not persuasive. The variants fails to meet USPTO written description guidelines because the invention as claimed fails to recite any functional limitation associated with structural variants as claimed. Furthermore the specification defines that the AAV4 capsid polypeptide is encoded by ORF 2 of AAV4, comprising the amino acid sequence encoded by nucleotides 2260-4467 of the nucleotide sequence set forth in SEQ ID NO:1, or a unique fragment of such protein wherein the scope of AAV4 capsid protein further encodes variant of VP1, VP2 and VP3 (i.e. SEQ ID nO:4, 16 and 18). The specification clearly states that an AAV4 Capsid polypeptide including all three coat proteins will have at least about 63% overall homology to the polypeptide encoded by nucleotides 2260-4467 of the sequence set forth in SEQ ID NO:1 (see

spec. page 13-15). Therefore the AAV4 capsid protein and/or any variant thereof has not been claimed reciting any structural limitation associated with a function. As stated earlier the specification fails to disclose representative number of species by structure and function encompassed by genus as claimed. Furthermore the genus as claimed encompasses structurally and functionally distinct members. Claiming all divergent species that achieve a result as contemplated by the application without defining the representative number of species by structure and function is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. "The written description requirement has several policy objectives. The essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re Barker, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977).

In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e conserve motifs or domains). As stated earlier the art at the time of filing teaches that AAV4 has considerable homology with AAV2 and AAV3 (Chiorini et al J. Virol, 71(9):6823-33, 1997, see abstract, figure-1, figure-3, ref of record on PTO-1449). Therefore it is unclear how one skill in the art could possibly know what are the characteristic of AAV4 unless one skill in the art knows all known AAV-sequences and AAV sequences yet to be discovered in this context. In this case applicant only disclosed AAV4 (SEQ ID NO:1 nucleotides 2260-4467) and proposes to discover other members of the genus using a hybridization procedure. Another objective is to put the public in possession of what the applicant claims as the invention. See Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998)." To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the

claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention as claimed is "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention (January 5, 2001 Fed.Reg., Vo.66, No. 4, pp. 1099-11).

Since the specification fails to disclose a representative number of species defined by structure and function, it is not possible to envision the claimed composition. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).*

In the instant case the AAV4 capsid protein and its variants as claimed has been defined only by a statement of function that broadly encompasses having any and all characteristic of AAV4, which conveyed no distinguishing information about the identity of the claimed genetic material, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of even a single member of this genus would not be representative of other nucleic acid constructs genus and is insufficient to support the claim.

Claims 1-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AAV4 capsid protein encoded by the nucleotide sequences 2260-4467 of SEQ ID NO:1, does not reasonably provide enablement for any other variant of AAV4 capsid protein encoded by any nucleotide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the same reasons of record as set forth in the office action mailed on 06/28/06.

**Response to argument (Enablement)**

The applicant argues that for the reasons stated for written description, the Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

However this is found not persuasive in view of written description rejection above as the specification fails to disclose a representative number of species defined by structure and function (any nucleotide that have any and all characteristic of AAV4, variants of AAV4 rep and capsid proteins). Therefore, it is unclear how one skilled in the art use the invention as claimed (supra). The applicant's disclosure does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires the identification and characterization of any and all nucleic acid sequences any and all vectors systems or required to produce a vector system having any and all characteristic of AAV4. As stated above the art at the time of filing teaches that AAV4 has considerable homology with AAV2 and AAV3 (Chiorini et al J. Virol, 71(9):6823-33, 1997, see abstract, figure-1, figure-3, ref of record on PTO-1449). The disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Therefore it is unclear how one skill in the art could possibly know what are the characteristic of AAV4 unless one skill in the art knows all known AAV-sequences and AAV sequences yet to be discovered in this context. In this case applicant only disclosed AAV4 genome (AAV4 2260-4467nt of SEQ ID NO:1), AAV4 Rep proteins (SEQ ID NO(s): 2, 8, 9, 10 and 11) and AAV4 Capsid proteins (SEQ ID NO(s): 4, 16

and 18); and proposes to discover other members of the genus using a hybridization procedure. At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

***Claim Rejections - 35 USC § 102***

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Muser et al (Virlogy 35(3):653-61, 1980), for the same reasons of record as set forth in the office action mailed on 06/28/06.

Given the broadest reasonable interpretation the scope of invention as claimed encompasses an isolated nucleic acid encoding an AAV4 capsid protein.

Muster teaches isolation of AAV4 DNA and physical mapping of the AAV4 genome, which clearly comprises a nucleotide sequence encoding an AAV4 capsid protein and have the characteristic of AAV4 (page 653, abstract, col.1 para.1). Muster teaches isolation of AAV4 virions from the host cells, followed by isolation of AAV4 DNA from the purified virions (page 654, col.1 para.3-4). Thus the cited art clearly anticipate the invention as claimed because the composition and functions as claimed are presumed inherent in the prior art regarding AAV DNA. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the

properties applicant discloses and/or claims are necessarily present. See In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02.

**Response to argument (Anticipation)**

The applicant argues that instant claim has been amended to recite claim limitation "an isolated nucleic acid encoding an AAV4 protein, which means that invention as claimed does comprises the entire AAV genome. The applicant further argues that Muster et al. did provides no AAV4 sequences, thus providing no chemical structure for any AAV4 sequence to be use in vector. The applicant argues that in order to utilize the AAV4 genome and its subsequences as vectors, it was necessary to isolate and sequence an exemplary AAV4 genome to determine whether or not it could be used as a vector.

However, this is found not persuasive because the invention as claimed is not limited to a particular set of nucleotide sequences. In addition the invention as claimed is drawn a vector comprising an isolated nucleic acid sequence encoding any AAV4 capsid protein. Muster teaches clearly isolation of AAV4 DNA and physical mapping of the AAV4 genome, which clearly comprises a nucleotide sequence encoding an AAV4 capsid protein and have the characteristic of AAV4 (page 653, abstract, col.1 para; page 654, col.1 para.3-4). Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

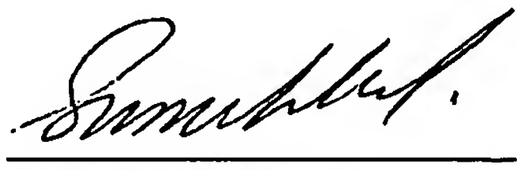
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



**SUMESH KAUSHAL**
**PRIMARY EXAMINER**